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08/982,272

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/982,272	12/01/97	KIPPS	T 231/003

EXAMINER

HM22/1012

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ART UNIT	PAPER NUMBER
1644	14

DATE MAILED: 10/12/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 7/12/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-83 is/are pending in the application.
Of the above, claim(s) 11-66, 68-82 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1-10, 67, 83 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e). SEE ACTION

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 13
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. Applicant's amendment, filed 7/19/99 (Paper No. 12), is acknowledged.

Claims 1-10, 67 and 83 are being acted upon as the elected invention.

Claims 11-66, 68-82 and the non-elected species have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 7/19/99 (Paper No. 12). The rejections of record can be found in the previous Office Action (Paper No. 9).

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because it does not provide for 119(e) priority to the provisional application 60/032145.

Applicant's amendment, filed 7/1/9/99 (Paper No. 12), indicates that the Declaration hs been changed to comply with 37 CFR 1.67(a). However, no such Declaration appears attached to applicant's amendment. The examiner apologizes for any inconvenience to applicant, but the only Declaration in the instant file application is defective for the reasons of record and herein.

4. Applicant is reminded to amend the first line of the specification to correct the serial number of the provisional application relied upon for priority. The serial number should be 60/032145

5. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).

Applicant's arguments, filed 7/19/99 (Paper No. 12), indicates that in conjunction with arguments addressing the 35 USC 112, second paragraph, rejection indicates that the Abstract is suitably descriptive of the claimed invention. However, the Abstract does not disclose the particular or elected species of accessory molecule ligands.

6. This application has been filed with informal drawings which are acceptable for examination purposes only.

7. Applicant's arguments, filed 7/19/99 (Paper No. 12), indicates that the various objections and informalities indicated in Paper No. 9 be held in abeyance pending notification of allowable subject matter.

8. Claims 1-7, 67, 83 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments, filed 7/19/99 (Paper No. 12), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 9.

Applicant argues that the term "ligand" used in the instant claims does not appear in a vacuum, but should be read in the context of "accessory molecule"; which have a meaning both in the art as well as the specification (e.g. page 2 of the specification). Here, applicant relies upon "an accessory molecule ligand" that is present on another/different cell type -- intercellular reaction. Applicant also relies upon the prior art references (Alderson et al., 1993; Yellin et al., 1994; Freeman, '310 patent), in order to distinguish accessory molecule ligands from cognate accessory molecules to indicate that "accessory molecule" or costimulatory molecule" have definite, distinct and well known meaning in the art.

In addition applicant argues in conjunction with In re Wands , PPG Industries, Inc. V. Guardian Industries Corp. In re Certain Limited-Charge Cell Culture Microcarriers and the specification, to indicate that it would not be undue experimentation to enable the scope of the claimed invention. For example, applicant relies upon various recombinant methods as well as the guidance and direction in the specification as filed to support enablement

The following of record is reiterated with respect to the 35 U.S.C. § 112, first and second paragraphs, issues with respect to "accessory molecule ligand".

The instant claims are indefinite in the recitation of "an accessory molecule ligand" because the characteristics of the "ligand" are ambiguous and unclear. This language is vague and indefinite since it encompasses a myriad of molecules. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the "an accessory molecule ligand" encompassed by the claimed invention. While page 20 of the instant specification discloses that "an accessory molecule ligand" refers to members of TNF family; the art recognizes a number of different molecules that serve as "an accessory molecule ligand" (e.g. members of the B7 : CD28 family of costimulatory molecules). The recitation of "an accessory molecule ligand" fails to distinctly claim what that protein is and what the compositions are made up of. Further, it is noted that "ligand" can be considered a relative term in that with receptor-ligand interactions, whether a molecule is the ligand or the receptor can be a matter of perspective or point of reference (e.g. CD40 ligand is a ligand for CD40; CD40 is a ligand for CD40 ligand).

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of "an accessory molecule ligand organic molecules" commensurate in scope with the claimed invention nor is there sufficient evidence provided that any "accessory molecule ligand" including all members of the disclosed TNF family could be used to alter the immunoreactivity of a cell including tumor cells. It would require undue experimentation to produce all such possible "accessory molecule ligands" without more explicit guidance from the disclosure. It would require undue experimentation to investigate all such "accessory molecule ligands". Applicant has failed to enable or provide written description for nucleic acids encoding a myriad of "accessory molecule ligands" and fails to provide sufficient guidance to those skilled generally on how to make and use "accessory molecule ligands", commensurate in scope with the claimed invention to alter immunoreactivity of cells. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods to alter immunoreactivity of cells with "accessory molecule ligands", commensurate in scope with the claimed invention.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

Applicant's arguments are not found persuasive.

9. Claims 1-8, 10 and 83 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Yellin et al. (J. Immunol., 1994) for the reasons of record set forth in Paper No. 9.

Applicant's arguments, filed 7/19/99 (Paper No. 12), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 9. Applicant argues that fails to note any mention of transfection in this reference. However, this reference relies upon the T-BAM/CD40L expressing or transfected D1.1 cell line (as well as the B2.7 clone) (see Materials and Methods, Cell Lines). Therefore, this reference teaches altering the immunoreactivity of human cells encoding an accessory molecule ligand. Applicant's arguments are not found persuasive.

10. Applicant's arguments, filed 7/19/99 (Paper No. 12), indicating that the CV-1 cells of Alderson et al. are primate but not human cells has obviated the previous rejection under 35 U.S.C. § 102(b) as being anticipated by Alderson et al. (J. Exp. Med., 1993).

11. Claims 1-7, 67 and 83 are rejected under 35 U.S.C. § 102(e) as being anticipated by Freeman et al. (U.S. Patent No. 5,861,310) for the reasons of record set forth in Paper No. 9.

Applicant's arguments, filed 7/19/99 (Paper No. 12), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 9. Applicant argues that the characterization of the reference cannot be confirmed or accepted. However, applicant acknowledges that Freeman teaches transgenic supply of B/APC cell accessory molecules (B7, B7-2 and B7-3) and not corresponding ligands (e.g. CD28 or CTLA-4), which are distinguishable. Applicant also asserts that the references teach transfection of cells with genes that encode accessory molecule that are characteristic of normal expression in those very cell types; while the instant invention teaches useful transfection of accessory molecule ligands genes that are not normally of functionally expressed in cells which express the corresponding and complementary accessory molecules.

As pointed out previously, that although it was acknowledged that CD40 ligand is the elected species, this reference, which is used in the obviousness rejection below, anticipates the claimed methods.

In contrast to applicant's inability to confirm or accept the characterization of the teaching of Freeman et al; this reference is replete with teaching transfecting human cells with costimulatory molecules and claims encompassing cells transfected with costimulatory molecules (for example, see entire document, including Summary of the Invention, Detailed Description of the Invention, Ex Vivo Modification of a Tumor Cell to Express a Costimulatory Molecule, Transfection of a Tumor Cell with a Nucleic Acid Encoding a Costimulatory Molecule).

Further, applicant appears to argue limitations not claimed. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). See MPEP 2145.

Also, the phrase "accessory molecule ligand" does not restrict the claims to an accessory molecule such as B7 versus it corresponding ligand such as CD28 because it is a matter of perspective as to which member of a receptor-ligand pair is the receptor of the ligand. Given the ambiguity as to the metes and bounds or the lack of distinctly defining an "accessory molecule ligand"; the claimed "accessory molecule ligand" is not limited to one member of a receptor-ligand pair over the other.

Applicant's arguments are not found persuasive.

12. Claims 1-10, 67 and 83 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Freeman et al. (U.S. Patent No. 5,861,310) in view of Yellin et al. (J. Immunol., 1994) and Alderson et al. (J. Exp. Med., 1993) as well as pages 40-53 of the instant specification for the reasons of record set forth in Paper No. 9.

Applicant's amendment, filed 7/19/99 (Paper No. 12), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 9. Given the lack of additional arguments addressing this rejection under 35 U.S.C. § 103(a) other than the reliance on addressing these references as they apply in the rejection under under 35 U.S.C. § 102; the previous obviousness rejection is maintained and reiterated herein for applicant's convenience.

The instant claims are drawn to methods of altering the immunoreactivity of human cells or treating human neoplasia by inserting CD40L

Freeman et al. teach altering the reactivity of a cell and treating human neoplasia by introducing a gene encoding an accessory molecule ligand (B7) alone or together, that is to be expressed on a cell surface, including tumor cells (see entire document). Freeman et al. differs from the instant elected invention by not disclosing CD40 ligand as a costimulatory or accessory molecule

Yellin et al. teach that transfecting cells, including leukemia cells, with CD40 ligand enhances a cell costimulatory activity, including the priming and clonal expansion of antigen specific T cells as well as providing helper function for cytotoxic T cell responses (see entire document, including the Abstract and Discussion).

Alderson et al. teach that CD40 ligand transfected cells induce monocytes to become tumoricidal against human melanoma cells, which indicated that the CD40 ligand had potent biological effects (see entire document, including the Abstract and Discussion). Alderson et al. Teaches transfection with either murine or human CD40 ligand (for example, see page 671).

Therefore, it would have been prima obvious to the ordinary artisan at the time the invention was made to substitute the potent costimulatory/accessory molecule properties of the CD40 ligand into the methods of Freeman et al. to alter the immunoreactivity of cells, that is, to increase antigen presentation and/or immunoreactivity. The claimed limitations encompassing chimeric genes and vectors were known and practiced by the ordinary artisan at the time the invention was made, as evidenced by Freeman et al. Pages 40-53 of the instant specification also acknowledges that the general methods of providing chimeric/gene therapy constructs as well as manipulating cells for were known and practiced at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have been motivated to select CD40 ligand as an accessory molecule ligand to express in cells, including tumor cells, to increase their immunoreactivity. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

13. No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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